BIOGRAPHICAL SKETCH

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NAME OF SPONSOR (CO-SPONSOR)	POSITION TITLE
John M. Coffin	American Cancer Society Research Professor
eRA COMMONS USER NAME	
jcoffin1	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	YEAR(s)	FIELD OF STUDY
Wesleyan University, Middletown CT	BA	1967	Biology
University of Wisconsin, Madison WI	Ph.D.	1972	Molecular Biology
Institut für Molekularbiologie, University of Zürich		1972-1975	Molecular Virology

A. Personal Statement

I have studied basic aspects of retrovirus biology for more than 40 years, since 1975 as a member of the Tufts Basic Science Faculty. I have closely followed the HIV field ever since discovery of the virus in 1983, although I did not take an active role until I founded the NCI's HIV Drug Resistance Program in 1997. In 1995, I published an essay in which I pointed out that HIV must have a uniquely dynamic mechanism of persistence in the infected human host, and argued that drug resistance must arise during replication, and are then selected from the highly divers population, often leading to therapeutic failure. The invitation to start a new research program within the NCI dedicated to the study of HIV-host interaction allowed me to put together a group to develop a set of uniquely sensitive and specific assays to quantitatively assess viral diversity, persistence, and evolution of resistance in infected patients. All of the assays developed by this group, including particularly single genome sequencing and allele-specific PCR,900 have become the gold standard in the field for studying HIV-host interaction, and their use has provided significant insight into mechanisms of its replication, persistence, and evolution. At the same time, I have continued to delve into important theoretical aspects of HIV infection, such as the roles of immune selection and recombination in evolution in vivo. Listed below are a small fraction of my publications on these topics.

B. Positions and Honors

Professional Experience:

1972-1975 Postdoctoral Fellow, Institut für Molekularbiologie, Universitat Zürich
1975-1978 Assistant Professor, Molecular Biology and Microbiology, Tufts University School of Medicine
1978-1982 Associate Professor, Molecular Biology and Microbiology, Tufts University School of Medicine
1982-present Professor, Molecular Biology and Microbiology, Tufts University School of Medicine
1985-1994 American Cancer Society, Massachusetts Division, Professor of Molecular Biology
1994-present American Cancer Society Research Professor of Molecular Biology and Microbiology
2002-present Distinguished Professor, Tufts University
1997-2005 Director, HIV Drug Resistance Program, National Cancer Institute, Frederick MD

Honors and Service

Fellow, Jane Coffin Childs Memorial Fund for Medical Research, 1972-74
Editorial Boards: J. Virol. 1978-1991, Virology, 1980-1993, Genes and Development, 1991-1994, PNAS, 2000-
Editor, Journal of Virology, 1991-1997
Virology Study Section, 1980-1984
Organizer, Cold Spring Harbor meeting on RNA Tumor Viruses, 1981, 1991, 1997

Member, Retrovirus subsection, International Committee on the Taxonomy of Viruses, 1982-1987, Chair, 1987-95
Member, California AIDS Task Force, Basic Science Review Group, 1986-97, Chair 1993-97
Member, Leukemia Society of America, Grant Review Subcommittee, 1987-1991; 1992-2000, Chair 1997-2000
Member, Leukemia Society of America, National Board of Trustees, 1987-1991, 1992-2004
Member, National Cancer Institute Manpower Initial Review Group, 1987-1991
Outstanding Investigator Award, National Institutes of Health, 1987-1994; 1994-2001
Reviewing Editor, Science, 1987- 1996
American Society for Microbiology Foundation Lecturer, 1988-1989
Member, Institute of Medicine Committee to Study the AIDS Research Program of the NIH, 1989-1991
Milton and Natalie Zucker Award for Research, 1989, 1997
Member, National Cancer Institute-Frederick Cancer Research & Development Center Advisory Committee, 1993-1997
Fellow, American Academy of Microbiology, 1993-present
Member, Panel to Assess the NIH Investment in Gene Therapy, 1995
Distinguished Faculty Award, Tufts University, 1997
Member, National Academy of Sciences, 1999-
Massachusetts Columbus Quincentennial Discovery Award, 2006
Member, Massachusetts Academy of Sciences, 2008-

C. Selected Publications (out of about 150 total)

5 Most relevant Publications:

Coffin, J.M. 1995. HIV population dynamics in vivo: Implications for genetic variation, pathogenesis, and therapy. Science 267: 483-488.

Palmer S, Maldarelli F, Wiegand A, Bernstein B, Hanna GJ, Brun SC, Kempf DJ, Mellors JW, Coffin JM, and King MS. 2008 Low-level viremia persists for at least seven years in patients on suppressive antiretroviral therapy. PNAS. 105: 3879-3884.

Batorsky, R., Kearney, M.F., Palmer, S.E., Maldarelli, F., Rouzine, I.M., and Coffin, J.M. 2011, Estimate of effective recombination rate and average selection coefficient for HIV in chronic infection. PNAS. **108:** 5661-5666.

Josefsson, L, King, M. S., Makitalo, B., Brännström1, J. , Shao, W., Maldarelli, F., Kearney, M., Hu, W-S., Chen, J. Gaines1, H., Mellors, J., Albert, J., Coffin, J. M*., and S. Palmer*. 2011. Single cell analysis reveals that the majority of CD4+ T-cells from peripheral blood of HIV-1 infected individuals contain only one HIV DNA molecule. PNAS **108:** 11199-11204**.**

Paprotka,T*., Delviks-Frankenberry,K.A.*, Cingöz, O.,*, Martinez. A., Kung, H-J., Tepper, C.G., Hu, W.S., Fivash, Jr., M.J., Coffin, J.M., and Pathak, V.K. 2011. Recombinant Origin of the Retrovirus XMRV. Science. **333:** 97-101**.**

Other Relevant Publications:

Rouzine, I.M., Wakely, J., and Coffin, J.M. 2003. The solitary wave of asexual evolution. Proc. Natl. Acad. Sci. USA 100: 587-592.

Maldarelli, F., Palmer, S., King, M.S., Wiegand, A., Polis, M.A., Mican, J., Kovacs, J.A., Davey, R.T., Rock-Kress, D., Dewar, R., Liu, S, Metcalf, J.A., Rehm, C., Brun, S.C., Hanna, G.J., Kempf, D.J., Coffin, J.M., Mellors, J.W. 2007. Suppressive antiretroviral therapy lowers plasma HIV-1 RNA to stable set-point predicted by pretreatment viremia but not treatment regimen. PloS Pathog

Ambrose,Z., Palmer, S., Boltz, V.F., Kearney, M., Larsen, K., Polacino, P., Flanary, L., Oswald, K., Piatak, Jr., M., Smedley, J., Shao, W., Bischofberger N., Maldarelli, F., Kimata, J.T., Mellors, J.W., Hu, S.-L., Coffin, J.M., Lifson, J.D. and KewalRamani, V.N. 2007 Suppression of viremia and evolution of human immunodeficiency virus type 1 drug resistance in a macaque model for antiretroviral therapy..

Kearney M, Maldarelli F, Shao W, Margolick JB, Daar ES, Mellors JW, Rao V, Coffin JM, Palmer S. 2009. HIV-1 Population Genetics and Adaptation in Newly Infected Individuals. J. Virol.**83:** 2715-2727

Dinoso, J. B, Kim, S. Y, Wiegand, A. M., Palmer, S. E., Gange, S. J., Cranmer, L., O'Shea, A., Callender, M., Spivak, A., Brennan, T., Kearney, M. F., Proschan, M. A., Mican, J. M., Rehm, C. A., Coffin, J. M.,

Mellors, J. W., Siliciano, R. F., Maldarelli, F. 2009. Treatment Intensification Does Not Reduce Residual HIV-1 Viremia in Patients on highly Active Antiretroviral Therapy. PNAS. **106:** 9403-9408

Rouzine, I.M. and Coffin, J.M. 2010. Multi-Site Adaptation in the Presence of Infrequent recombination. Theor Popul Biol **77**: 189-204.

Horie M., Honda T., Suzuki Y., Kobayashi Y., Daito T., Oshida T., Ikuta K., Jern P., Gojobori T., Coffin J.M., and Tomonaga K. 2010. Endogenous non-retroviral RNA virus elements in mammalian genomes. Nature **463:** 84-87.

Mens, H., Kearney, M., Wiegand, A., Shao, W., Schonning, K., Gerstoft, J., Obel, N., Maldarelli, F., Mellors, J. W., Benfield, T. and Coffin, J. M. 2010. HIV-1 Continues to Replicate and Evolve in Patients with Natural Control of HIV infection. J Virol. **84**:12971-12981.

Gandhi, R. T., Zheng, L., Bosch, R. J., Chan, E. S., Margolis, D. M., Read, S., Kallungal, B., Palmer, S., Medvik, K., Lederman, M. M., Alatrakchi, N., Jacobson, J. M., Wiegand, A., Kearney, M., Coffin, J. M., Mellors, J. W. and Eron, J. J. 2010. The effect of raltegravir intensification on low-level residual viremia in HIV-infected patients on antiretroviral therapy: a randomized controlled trial. *PLoS Med* **7**. ePub Ahead of Print.

Kearney, M., Spindler, J., Shao, W., Maldarelli, F., Palmer, S., Hu, S. L., Lifson, J. D., Kewalramani, V. N., Mellors, J. W., Coffin, J. M. and Ambrose, Z. 2011. Genetic Diversity of Simian Immunodeficiency Virus Encoding HIV-1 Reverse Transcriptase (RT-SHIVmne) Persists in Macaques Despite Antiretroviral Therapy. J Virol. **85:** 1067-1076.

Boltz, V.F., Zheng,Y., Lockman, S., Hong, F., Halvas, E.K., McIntyre, J.A., Currier, J.S., Chibowa, M.C., Kanyama, C., Nair, A., Owino-Ong'or,W., Hughes, M.D., Coffin, J.M., and J.W. Mellors. 2011 Role of Low-Frequency HIV-1 Variants in Failure of Nevirapine-Containing Antiviral Therapy in Women Previously Exposed to Single Dose Nevirapine. PNAS. **108:** 9202-9207

Subramanian, R. P., Wildschutte, J. H., Russo, C. and Coffin, J. M. 2011. Identification, characterization, and comparative genomic distribution of the HERV-K (HML-2) group of human endogenous retroviruses. Retrovirology **8**: 90.

Cingöz, O., Paprotka, T., Delviks-Frankenberry, K.A., Wildt, S. Hu, W.-S. Pathak, V. K., and Coffin J M. 2011. Characterization, Mapping and Distribution of the Two XMRV Parental Proviruses. J. Virol. **86**: 328-338**.**

Paprotka,T*., Delviks-Frankenberry,K.A.*, Cingöz, O.,*, Martinez. A., Kung, H-J., Tepper, C.G., Hu, W.S., Fivash, Jr., M.J., Coffin, J.M., and Pathak, V.K. 2011. Recombinant Origin of the Retrovirus XMRV. Science. **333:** 97-101**.**

Tipper, C. H., Cingoz, O. and Coffin, J. M. 2012. Mus spicilegus endogenous retrovirus HEMV uses murine sodium-dependent myo-inositol transporter 1 as a receptor. J Virol. **86:** 6341-6344.

Henzy, J. E., and J. M. Coffin**.** 2013. Betaretroviral envelope subunits are noncovalently associated and restricted to the mammalian class. J Virol **87:**1937-1946.

* Equal contribution

C. Research Support

Ongoing Research Support

R37 CA089441 Coffin (PI) (30%) 02/01/06 – 01/31/16
NIH/NCI
Retrovirus Evolution
Overall goals: To study important problems in retrovirus evolution, including roles of mutation, drift, recombination, and selection in short term evolution of viruses, evolution of *env* genes to use different receptors, and the long-term relationship of retroviruses and their hosts as revealed by analysis of endogenous proviruses.

PRD94-037-13 Coffin (PI) 01/01/2008-4/30/2014
American Cancer Society
Research Professorship: Molecular Biology of Retroviruses
This award provides partial salary support for Dr. Coffin without supporting any specific projects